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Short-Term Morbidity of the Upper Limb after Sentinel Lymph Node Biopsy or Axillary Lymph Node Dissection for Stage I or II Breast Carcinoma

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BACKGROUND. The goals of sentinel lymph node biopsy (SLNB) are to improve axillary staging and reduce unnecessary axillary lymph node dissections (ALND), thereby reducing treatment-related upper-limb morbidity. In the current prospective study, short-term upper-limb morbidity was assessed after SLNB and/or ALND.

METHODS. The study comprised 204 patients with Stage I/II breast carcinoma. Mean patient age was 55.6 years (standard deviation, 11.6). Sixty-six patients (32%) underwent SLNB only, and 138 (68%) underwent a Level I–II ALND. Assessment (preoperative [t0] and 6 weeks postoperative [t1]) included evaluation of shoulder range of motion, muscle strength, grip strength, pain, upper/forearm circumference, shoulder disability, and activities of daily life (ADL).

RESULTS. Considerable treatment-related upper-limb morbidity was observed. Significant ($P < 0.001$) changes were found for pain, range of motion in forward flexion, abduction and abduction/external rotation, strength of shoulder abductors and elbow flexors, and in perceived disability in ADL. However, no significant difference in change of upper-limb function and ADL was found between the SLNB and ALND groups.

CONCLUSIONS. Significant short-term treatment-related upper-limb morbidity exists after SLNB or ALND. There is no significant difference in short-term treatment-related morbidity between SLNB and ALND. ***Cancer*** **2003;98:690–6.**

KEYWORDS: breast carcinoma, staging, sentinel lymph node, morbidity, activities of daily life.

The incidence of breast carcinoma in The Netherlands is 100 per 100,000 women per year.[1] Of every 10 women, 1 will develop breast carcinoma and 79% will survive at least 5 years.[1–2]

The goals of breast carcinoma treatment are local tumor control, optimal lymph node staging with minimal treatment-related morbidity, good functional results, and breast preservation. Axillary lymph node status is the most significant prognostic variable in patients with breast carcinoma.[3–6] Therefore, axillary lymph node dissection (ALND) is an important diagnostic, staging, and treatment procedure.[7] However, ALND may result in upper-limb morbidity such as pain, numbness, lymph edema, weakness, and impaired shoulder range of motion.[7–14] Upper-limb morbidity may interfere with the activities of daily life (ADL) and quality of life.[13–21] In the early postoperative period, return to routine activities is usually difficult because of pain and restricted range of motion of the shoulder.[22,23] The sentinel lymph node procedure was introduced recently to decrease

the number of unnecessary ALNDs and to reduce surgery-related morbidity as a result of ALND.[24–27] Sentinel lymph node biopsy (SLNB) removes selectively the lymph node that receives the metastatic drainage from the tumor. SLNB is an accepted procedure because of its accuracy to predict the presence of metastatic disease in the axillary lymph nodes.[24,25,28,29] Yet, to our knowledge, only a few studies have been performed to evaluate morbidity after SLNB.[26,27,29–35] Follow-up in these studies was less than 2 years and SLNB-related morbidity seemed to be less in comparison to ALND-related morbidity.[26,27,30–35]

Although the number of studies investigating upper-limb morbidity after breast carcinoma is increasing, the role of SLNB in reducing upper-limb morbidity and perceived disability in all postoperative phases is still not clear.[27,30,32] The aim of the current study was to analyze prospectively the short-term upper-limb morbidity and perceived disability in ADL of patients after SLNB versus ALND.

MATERIALS AND METHODS

From June 1999 to June 2001, patients with Stage I (T1N0M0: tumor 2 cm or less in greatest dimension [T1], no regional lymph node metastasis [N0], no distant metastasis [M0]) or Stage II (T1N1M0, T2N0M0, T2N1M0, T3N0M0: metastasis to movable ipsilateral axillary lymph node [N1], tumor more than 2 cm but not more than 5 cm in greatest dimension [T2], tumor more than 5 cm in greatest dimension [T3]) breast carcinoma participated in a cohort study to assess treatment-related upper-limb morbidity.[36] Patients were retrieved from two hospitals. The Groningen University Hospital already had been using SLNB in its staging procedure whereas the Martini Hospital Groningen introduced SLNB halfway during the inclusion period. Informed consent was obtained from the participating patients. The protocol was approved by the institutional review board committees of both institutions. Data regarding patient characteristics and treatment variables were collected from the medical records. Two groups of patients were distinguished in the current study: patients who underwent SLNB and patients who underwent ALND or ALND after SLNB. Sentinel lymph nodes were identified using both a radioactive tracer and Patent blue dye (Blue Patenté II; Labatoire Guerbet, Aulnay-sous-Bois, France). If metastases were identified in the sentinel lymph node, ALND was performed within 2 weeks after the SLNB. The procedure has been described extensively by Rutgers et al.[37] ALND consisted of a Level I–II axillary dissection. Contemporary surgical treatment included a modified radical mastectomy or breast-conserving treatment.

TABLE 1
Assessment of Shoulder Function and Activities of Daily Life

Assessment	Assessment tool
Shoulder function	
Pain (current pain)	VAS[a] (cm)
Numbness	Clinical examination: numbness (yes or no)
Active shoulder range of motion	
Forward flexion	Isomed inclinometer[b] (°)
Abduction	Isomed inclinometer[b] (°)
External rotation	Isomed inclinometer[b] (°)
Combined abduction/external rotation	Isomed inclinometer[b] (°)
Muscle strength	
Shoulder abductors	Citec hand-held dynamometer. (Newton-meters)[c]
Elbow flexors	Citec hand-held dynamometer (Newton-meters)[42–44]
Grip strength (cylinder grip)	Yamar hand-dynamometer (Newton-meters)[d]
Upper arm circumference	10 cm proximal to the olecranon[e]
Fore arm circumference	15 cm proximal to the processus styloideus ulnae[e]
ADL	SDQ[f] and GARS[g]

VAS: visual analog scale; cm: centimeters; °: degrees; ADL: activities of daily life; SDQ: Shoulder Disability Questionnaire; GARS: Groningen Activity Restriction Scale.
[a] See Hladink et al., 1992,[38] and Jensen et al., 1986.[39]
[b] See Gerber et al., 1992,[40] and Green et al., 1998.[41]
[c] See Van der Ploeg, 1992[42]; Van der Ploeg et al., 1991[43]; and Balogun et al., 1998.[44]
[d] See Swedborg et al., 1981,[15] and Mathiowetz et al., 1984.[45]
[e] Measured with the Gulick measuring tape (Lafayette Instruments, model 258-J00305).
[f] See Van der Heijden, 1996,[46] and Van der Heijden et al., 2000.[47]
[g] See Kempen et al., 1996,[48] and Suurmeijer et al., 1994.[49]

Upper-limb function and ADL were evaluated 1 day before surgery (t0) and 6 weeks after surgery (t1). Pain was assessed with a visual analog scale (VAS; Table 1). Patients were asked to mark their current pain perception on a 10 cm straight line (0 cm = no pain, 10 cm = worst pain imaginable).[38,39] Upper-limb function was assessed during a standardized physical examination (Table 1). Active shoulder range of motion was measured with a goniometer according to a standardized protocol in forward flexion, abduction, and external rotation.[40,41] The muscle strength of the shoulder abductors and elbow flexors was measured using a hand-held dynamometer (Citec; Groningen, The Netherlands)[42–44] and grip strength was measured with a Yamar (Bollingbrook, IL) hand-dynamometer.[15,45] All muscle strength measurements were performed three times and the mean of these three measurements was used for further analysis. Upper and forearm circumference was measured with a Gulick measuring tape at 10 cm proximal to the olecranon and 15 cm proximal to the processus styloideus ulnae.

ADL was assessed with the Shoulder Disability Questionnaire (SDQ) and the Groningen Activity Re-

striction Scale (GARS). The 16-item SDQ is a functional status measure that evaluates the ability of patients with shoulder disorders to perform daily activities.[46,47] The SDQ contains 16 statements that describe the situations in which patients experience pain and what some of the effects may be. It has a three-category response format (e.g., 1: *yes my shoulder is painful when I open or close a door*; 2: *no my shoulder is not painful when I open or close a door*; 3: *I did not perform the activity during the past 24 hours*). The total score for the 16 statements ranges from 0 (no functional status limitation) to 100 (maximum functional status limitation) (Table 1).[46,47] The GARS assesses the perceived restrictions (disability) in performing 18 ADL.[48,49] It has a four-category response format (1: *able to perform the activity without any difficulty*; 2: *able to perform the activity with some difficulty*; 3: *able to perform the activity with much difficulty*; 4: *unable to perform the activity independently*). The sum score ranges from 18 (the person can perform all the activities without any difficulty) to 72 (the person cannot perform any activity without the help of others; Table 1).[48,49]

Statistical analyses were performed using descriptive statistics and *t* tests for independent samples for between-group comparisons and *t* tests for dependent samples for within-group comparisons. Differences were accepted as significant if *P* values were less than 0.05.

RESULTS

During 2 years (1999–2001), 208 consecutive patients with invasive breast carcinoma entered the study. Their mean age was 55.6 years (standard deviation [SD], 11.6). Forty-two percent had Stage I disease (n = 87), 41% had Stage IIA disease (n = 86), and 17% had Stage IIb disease (n = 35). One patient was excluded from the study because she had a prophylactic mastectomy due to a positive family history for breast carcinoma. Three patients canceled follow-up appointments before t1. One patient was treated elsewhere, and the other two found the assessment protocol bothersome and chose to withdraw from the study.

Two hundred four patients completed preoperative and postoperative assessments. Initially, 124 (61%) patients underwent a SLNB. Of these patients, 58 (47%) had metastatic disease in the sentinel lymph node(s) and additional ALND was performed. Therefore, the study comprised 66 patients with SLNB (32%) and 138 patients with a Level I–II ALND (68%; Fig. 1).

Of the 66 patients with SLNB, 17 patients received a mastectomy (26%) and 49 patients received breast-conserving treatment (74%). In the ALND group (n = 138), 68 patients received a mastectomy (49%) and 70 patients received breast-conserving treatment (51%).

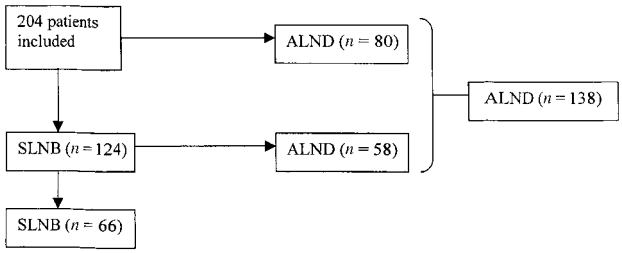

FIGURE 1. Diagram of patients included in the study. SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection.

Postoperative complications were scored in both groups. Serome production that lasted longer than 4 weeks was reported in 3 of 60 patients with SLNB (5%) and in 18 of 119 patients with ALND (15%; P = 0.051). Inflammation of the wound that necessitated antibiotic treatment occurred in 6 of 63 patients with SNLB (10%) and in 20 of 121 patients with ALND (17%), which was not significant (P = 0.265).

Significant treatment-related upper-limb morbidity and disability 6 weeks after surgery included pain, decreased range of motion in forward flexion, abduction, and abduction/external rotation, and loss of strength of shoulder abductors and elbow flexors (Table 2). The self-assessed perception of pain (VAS) increased from 0.5 (SD, 1.2) preoperatively to 1.3 (SD, 1.3) 6 weeks postoperatively ($P < 0.001$) (Table 2). One hundred thirty-eight patients(67.6 %) perceived postoperative numbness of the axillary region.

The largest decrease in range of motion of the shoulder was found in abduction (25.9 °, SD: 38.9) but there also was a significant decrease ($P < 0.001$) in the range of motion for forward flexion (11.2 °, SD: 21.2) and abduction/external rotation (8.2 °, SD: 17.4). No change in range of motion was observed for the external rotation alone. Considerably decreased muscle strength in the shoulder abductors (16.9 Newtonmeters [Nm]; SD, 52.3) and elbow flexors (15.1 Nm; SD, 58.9) was observed. Although grip strength decreased by 12.3 Nm (SD, 89.9) postoperatively, this decrease was not significant. The circumferences of the forearm and upper arm as measured 6 weeks after surgical treatment had not changed significantly (Table 2).

The SDQ and GARS found increased disability among the breast carcinoma patients. The change on the SDQ (15.4; SD, 34.6 [on a scoring range from 0–100]) was larger than the change assessed with the GARS (4.6; SD, 7.3 [on a scoring range from 18–72]) (Table 2).

TABLE 2
Upper-Limb Morbidity and Disability (t1–t0) 6 Weeks after Breast Carcinoma Treatment (n = 204)

	t0 (Preoperative)		t1 (6 wks postoperative)		Change (t1 − t0)		
Characteristic	Mean	SD	Mean	SD	Mean	SD	*P*
Pain (VAS: 0–10)	0.5	1.2	1.3	2.0	0.8	2.1	0.000
Forward flexion (°)	172.9	11.1	161.7	17.9	−11.2	21.2	0.000
Abduction (°)	168.1	21.6	142.2	34.1	−25.9	38.9	0.000
Abduction/external rotation (°)	87.1	6.5	78.9	16.0	−8.2	17.4	0.000
External rotation (°)	67.8	13.3	66.8	12.9	−1.0	18.5	0.414
Grip strength (Nm)	289.5	63.3	277.2	65.2	−12.3	89.9	0.059
Strength of shoulder abductors (Nm)	149.9	35.9	133.0	39.9	−16.9	52.3	0.000
Strength of elbow flexors (Nm)	178.8	42.0	163.7	41.3	−15.1	58.9	0.000
Circumference of upper arm (cm)	26.7	3.1	27.0	3.2	0.3	4.3	0.243
Circumference of forearm (cm)	24.2	2.1	24.3	2.2	0.1	2.9	0.484
SDQ (0–100)	8.7	20.2	24.1	30.2	15.4	34.6	0.000
GARS (18–72)	19.8	4.0	24.2	6.6	4.6	7.3	0.000

SD: standard deviation; VAS: visual analog scale; Nm: Newton-meters; cm: centimeters; °: degrees; SDQ: Shoulder Disability Questionnaire; GARS: Groningen Activity Restriction Scale.

TABLE 3
Changes in Upper-Limb Function and Disability in the Sentinel Lymph Node Biopsy and Axillary Lymph Node Dissection Groups: Results of *t* Tests for Independent Samples

	SLNB (t1 − t0) (n = 66)		ALND (t1 − t0) (n = 138)		Difference in mean change (ALND − SLNB)		
Characteristic	Mean change	SD	Mean change	SD	Mean difference	SD	*P*
Pain (VAS: 0–10)	1.1	2.1	1.3	2.0	0.2	0.3	0.528
Forward flexion (°)	−10.3	15.8	−11.5	23.4	1.2	2.9	0.680
Abduction (°)	−24.7	40.6	−26.4	38.4	1.7	6.0	0.774
Abduction/external rotation (°)	−7.2	13.1	−8.7	19.2	1.5	2.7	0.576
External rotation (°)	−2.1	19.3	−0.9	18.1	−1.2	2.9	0.670
Grip strength (Nm)	−5.8	94.1	−16.9	86.5	11.1	13.8	0.422
Strength of shoulder-abductors (Nm)	−15.9	55.8	−17.3	51.0	1.4	8.1	0.863
Strength of elbow-flexors (Nm)	−14.4	59.2	−15.5	59.1	1.1	9.2	0.907
Circumference of upper arm (cm)	0.9	4.2	0.1	4.3	−0.8	0.7	0.281
Circumference of forearm (cm)	0.4	3.1	0.0	2.9	−0.4	0.5	0.389
SDQ (0–100)	14.3	32.3	15.7	35.8	1.4	5.3	0.789
GARS (18–72)	3.5	7.2	4.9	7.5	1.4	1.1	0.191

SLNB: Sentinel lymph node biopsy; ALND: axillary lymph node dissection; SD: standard deviation; VAS: visual analog scale; Nm: Newton-meters; cm: centimeters; ° degrees; SDQ: Shoulder Disability Questionnaire; GARS: Groningen Activity Restriction Scale.

The increase in perceived disability between t0 and t1 was correlated significantly with the increase in pain (VAS) between t0 and t1 (Pearson correlation VAS_{t1-t0} and SDQ_{t1-t0} = 0.561, Pearson correlation VAS_{t1-t0} and $GARS_{t1-t0}$ = 0.422). Other aspects of upper arm morbidity (e.g., decreased shoulder range of motion and loss of strength) were not correlated significantly with an increase in perceived disability. None of the assessments of the noninvolved side changed significantly between t0 and t1.

Changes in upper-limb function (upper-limb morbidity) and ADL (perceived disability) between t0 and t1 were not significantly different between the SLNB group and the ALND group (Table 3). Although almost all assessed items of upper-limb function and ADL changed slightly more in the ALND group compared with the SLNB group, none of these differences were significant.

Numbness was observed in 42 patients in the SLND group (64%) and in 96 patients in the ALND group (70%) at t1 (P = 0.519). The changes in upper-limb function and ADL between t0 and t1 for patients

who received breast-conserving therapy or a modified radical mastectomy also were assessed (data not shown). No significant differences in upper-limb function and ADL were documented for these two groups. In a post hoc analysis, patients who underwent breast-conserving therapy ($n = 119$) were selected to analyze in a homogeneous group, the influence of SLNB and ALND on the outcome variables. In the *t* test for independent samples, no significant difference in change in upper-limb function or ADL was found between the groups (data not shown).

DISCUSSION

The current study showed that there is significant short-term upper-limb morbidity and associated ADL disabilities in patients with breast carcinoma who undergo SLNB and/or ALND. However, no significant differences in short-term upper-limb morbidity and ADL disabilities were found between the SLNB and ALND groups.

This outcome contradicts the assumption that SLNB, a much less extensive procedure compared with ALND, is associated with less upper-limb morbidity than ALND. To our knowledge, only three other studies have reported morbidity results after a relatively short follow-up period after SLNB and ALND.[32–34] Baron et al.[32] and Temple et al.[33] used a self-constructed instrument (i.e., the Breast Sensation Assessment Scale) to assess sensory morbidity. Although the authors reported some difference in prevalence of breast sensations between SLNB and ALND at baseline (3–15 days postsurgery) and 3 months postsurgery, the difference was significant for only 5 of the 18 sensations. When women reported sensations as severe or very severe, a significant difference in prevalence was only present for 3 of the 18 sensations (specifically, numbness, stiffness, and tingling).[32]

Swenson et al.[34] assessed the side effects of both procedures with a self- constructed questionnaire (i.e., the Measure of Arm Symptom Survey) at 1, 6, and 12 months postsurgery. They found significant differences in perceived pain, numbness, limitation in range of motion, and interference with daily life between patients with ALND and patients with SLNB at 1 month postsurgery. This difference in occurrence of side effects in favor of the SLNB patients continued at 6 and 12 months postsurgery, with the exception of interference in daily life.

In contrast to the three previous studies,[32–34] the current study used a preoperative baseline assessment. In addition, several reliable and validated objective assessment tools were used and the influence of short-term upper-limb morbidity on ADL was assessed.[15,38–49] In a recent systematic review,[14] the importance of the baseline assessment against which to compare the follow- up assessment was emphasized.[14] Using this baseline assessment, possible disturbances in the cause-and-effect relation were ruled out and therefore only the postoperative changes in upper-limb function and ADL were reported.

A potential limitation of the current study is that contemporary treatment options (mastectomy/breast-conserving surgery) were not divided equally between the SLNB and ALND groups. However, a post hoc analysis of the influence of SLNB and ALND on the outcome variables in only the breast-conserving treatment group showed no significant differences in the occurrence of upper-limb morbidity and ADL disabilities (data not shown). Other potential confounders such as adjuvant radiotherapy and chemotherapy had no influence on the study outcome because they were started after the postoperative (t1) assessment.

A power analysis was not performed before the study. However, if the small differences in change between the groups (SLNB and ALND) became significant in a much larger study, the clinical relevance of these small differences would be questioned. In addition, because the SLNB procedure is a relatively new technique, no data were available to perform an adequate power analysis before the current study.

No significant difference in the prevalence of numbness between the SLNB and ALND group was documented, which is in contrast to other studies.[26,32–35] The high numbness score among the SLNB patients cannot be explained.

A significant change in upper-limb function and ADL after SLNB or ALND was found in the current study. However, the overall upper-limb morbidity and associated disability in ADL was low. Specific shoulder-related disability in ADL (SDQ) was more affected than overall ADL (GARS). Pain was the only impairment that correlated significantly with perceived disability postsurgery (Pearson correlation VAS_{t1-t0} and $SDQ_{t1-t0} = 0.561$, Pearson correlation VAS_{t1-t0} and $GARS_{t1-t0} = 0.422$). Although there are significant but rather small mean differences in upper-limb function (e.g., decreased forward flexion, abduction, decreased strength of shoulder abductors and elbow flexors), these differences were not clinically relevant in relation to perceived disabilities in ADL 6 weeks postsurgery.

In conclusion, significant short-term treatment-related upper-limb morbidity and associated ADL disabilities exist after SLNB or ALND. There is no significant difference in short-term treatment-related morbidity between SLNB and ALND.

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